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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/038,192	DELMAS ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-19,22-28 and 30-32* is/are pending in the application.

4a) Of the above claim(s) *3-9,12,22,23,25-28 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,11,13-19,24,30 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed December 11, 2003 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 11, 13-19, 24, 30 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it recites a method of diagnosing or monitoring the evolution of a synovial disease. It is unclear which is being done. Further, diagnosing would involve a definitive yes or no for having the disease, whereas monitoring would involve determining a progression. Therefore, it is unclear how both are performed.

Claim 2 provides for the use of the method in claim 1, but, since the claim does not set forth any steps to differentiate such monitoring which is different from the method of diagnosing, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 32 provides for the use of the method of claim 1, but since the claim does not set forth any steps to differentiate such diagnosing which is different from the method of monitoring, it is unclear what method/process applicant is intending to

encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 2, 11, 13-16, 18 and 19 rejected under 35 U.S.C. 103(a) as being unpatentable over Blum et al (Detectable levels of pyridinoline are present in synovial fluid from various patients with knew effusion: preliminary results European Journal of Clinical Investigation (1995) Vol 25, No. 6, pp. 438-441) in view of Robins et al (WO 89/12824).

Blum et al disclose a method for early diagnosis of inflammatory joint diseases (synovial disease) such as rheumatoid arthritis and degenerative joint diseases such as osteoarthritis. Blum et al disclose measuring pyridinoline (marker). Blum et al disclose that pyridinoline is issued from the degradation of mature collagens in synovial tissue (p. 438). Blum et al disclose that the measurement is performed by high performance liquid chromatography (HPLC). Blum et al also disclose comparing the levels of pyridinoline with a knee effusion with post-traumatic effusion.

Blum et al differ from the instant invention in failing to teach the specific marker is glycosylated pyridinoline or diglycosylated pyridinoline.

Robins et al disclose the measurement of glycosylated pyridinoline and diglycosylated pryidinoline which have been shown to be present in increased amounts in arthritic disease (p. 4-6). Robins et al disclose that these markers are specific to a particular tissue of origin. Robins et al also disclose the use of antibodies directed toward the glycosylated pyridinoline and diglycosylated pyridinoline can be used in immunoassays for the diagnosis and monitoring of various types of degenerative joint disorders (p. 8).

It would have been obvious to one of ordinary skill in the art to incorporate glycosylated pyridinole or diglycosylated pyridinole as taught by Robins et al as the markers for the method of Blum et al because Robins et al shows that the use of glycosylated pyridinole or diglycosylated pyridinole provides markers that are specific to a particular tissue of origin. Further, Blum specifically teaches Pyridinole is increased in rheumatoid arthritis and Robins specifically teaches that glycosylated pyridinole and diglycosylated pyridinole are increased in arthritis disease (p. 6, lines 1-5). Therefore, it would have been obvious to one of ordinary skill in the art to detect glycosylated pyridinole and diglycosylated pyridinole markers for diagnosing a synovial disease. Because it is known in the art that increased levels of these specific markers are associated with arthritic disease and Robins specifically teaches that detection of these molecules provides for the diagnosis and monitoring of various types of degenerative joint disorders (p 8).

With respect to claim 2 as recited in the instant claims. Claim 2 provides the use of the method of claim 1 and since claim 1 does not differentially set forth step as to do such monitoring which is different from the method of diagnosing, the combination of Blum et al and Robins reads on the instantly recited claim.

5. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blum et al and Robins in view of Sinigaglia (Urinary and synovial pyridinium crosslink concentrations in patients with rheumatoid arthritis and osteoarthritis, Abstract & Annals of the Rheumatic Diseases (1995 Feb) 54 (2) 144-147).

See above for teachings of Blum et al and Robins.

Blum et al and Robins differ from the instant invention in failing to teach the reference level is selected to be in the range from about 5 nmole/nmole creatinin to about 9 nmole/nmole creatinin.

Sinigaglia teach that the concentration of Hydroxypyridinoline (HP) et Lysylpyridinoline (LP) are expressed as pmol/umol of creatinine in urinary samples (which is equivalent to nmol/mmol of creatinin). Further, as stated by applicant on page 12 of the remarks section filed December 11, 2003, that it is well known in the art to use creatinin as a standard reference. Therefore, it would have been obvious to one of ordinary skill in the art to incorporate creatinin as standard reference in the modified method of Blum et al.

6. Claims 24 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blum et al in view of Robins as applied to claims 1, 2, 11, 13-16, 18, 19 above, and further in view of Boguslaski et al (US 5,420,016).

See above teachings of Blum et al and Robins.

Blum et al and Robins differ from the instant invention in failing to teach packaging the components into a kit.

Boguslaski et al disclose assembling various system components into a test kit. By assembling these components into test kits, it makes it more convenient and facile for the test operator (col 7, lines 8-11).

It would have been obvious to one of ordinary skill in the art to package the reagents and components as taught by Blum et al and Robins into a kit because

Boguslaski et al teaches that assembling components into test kits, it makes it more convenient and facile for the test operator.

Response to Arguments

7. Applicant's arguments filed December 11, 2003 have been fully considered but they are not persuasive.

112 2nd Rejections

Applicant argues that claim 1 is clear and definite in that covers both diagnosis and monitoring. Applicant states that in the case of a diagnosis, the chosen reference level might be the mean level of a sample of healthy persons and that a determination that the value is higher than the reference would prompt a diagnosis of synovial disease, whereas a value that is about the same or lower than the reference would not result in such diagnosis. Applicant further states that in the case of monitoring the progression of a synovial disease, the chosen reference level might be the level of the specific marker that was previously determined and if the determined value is higher than the reference, one skilled in the art would understand this to mean that the synovial disease has progressed of if the value is lower than or unchanged from the reference, one skilled in the art would likely take this to mean that the synovial disease has not increased. This is not found persuasive because Claim 1 does not differentially set forth steps to do such monitoring which is different from method of diagnosing. Therefore, it is unclear which is being done.

Art Rejections

Applicant argues that there is no disclosure in Blum of measuring glycosylated pyridinoline to diagnose or monitor progression of a synovial disease. This is not found persuasive because Examiner has not relied upon Blum for teaching glycosylated pyridinole but rather has relied upon Robins for teaching increased levels of glycosylated pyridinole in arthritic disease.

Applicant argues that Blum et al is totally silent with respect to glycosylated pyridinoline or diglycosylated pyridinoline. Examiner agrees that Blum et al is silent with respect to glycosylated pyridinoline or diglycosylated pyridinoline. However, as stated above Examiner has not relied upon Blum for this teaching but rather has relied upon Robins for teaching glycosylated pyridinoline and diglycostlated pyridinoline as specific markers in arthritic diseases. Applicant further argues that Blum states that "pyridinium cross-link of collagen, pyridinoline (Pyr) and deoxypyridinoline (D-yr), are issued from the degradation of mature collagens of bone and cartilage." And that this statement is not indicative of, and thus would not have been suggestive of synovial collagen degradation. This is not found persuasive because Blum specifically teaches that pyridinoline released in SF originates from synovium (p 440).

Applicant argues that Robins does not remedy the deficiencies of Blum. Specifically, applicant argues that there is no disclosure in Robins of the use of glycosylated or di-glycosylated pyridinoline as markers specific for synovial disease. This is not found persuasive because Robins specifically teaches that glycosylated pyridinole and diglycosylated pyridinole are increased in arthritis disease (p. 6, lines 1-5). Applicant further argues that there is no mention or suggestion of synovail collagen

degradation. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., synovial collagen degradation) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that the collective teachings of Blum and Robins does not establish a case of *prima facie obviousness* and that the teachings of Boguslaski does not come close to the mark. This is not found persuasive because it is the Examiner's position that the combination of Blum and Robins teaches the limitations as recited and thus the combination with Boguslaki is appropriate.

Conclusion

8. No claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts

Gary Counts
Examiner
Art Unit 1641
March 9, 2004

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03/16/04